DISSERTATION ON

A STUDY ON
THE HEART DISEASES
IN
HIV POSITIVE PATIENTS

Submitted in partial fulfilment of

Requirements for

M.D. DEGREE BRANCH I GENERAL MEDICINE

Of

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI.

MADRAS MEDICAL COLLEGE

CHENNAI – 600 003.

MARCH – 2007

CERTIFICATE

This is to certify that this dissertation entitled "**A STUDY ON HEART DISEASES IN HIV POSITIVE PATIENTS**" submitted by **Dr.ARUN P.** appearing for M.D. Branch I General Medicine Degree examination in March 2007 is a bonafide record of work done by him under my direct guidance and supervision in partial fulfillment of regulations of the Tamil Nadu Dr.M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

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DECLARATION

I solemnly declare that the dissertation titled **"A STUDY ON HEART DISEASES IN HIV POSITIVE PATIENTS**" is done by me at Madras Medical College and Government General Hospital, Chennai during 2005-2006 under the guidance and supervision of Prof. V.K. Rajamani, M.D.

The dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

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SPECIAL ACKNOWLEDGEMENT

I gratefully acknowledge and sincerely thank **Prof.Dr.KALAVATHY PONNIRAIVAN, B.Sc., M.D.,** The DEAN, Madras Medical College and Government General Hospital, Chennai for allowing to do this Dissertation and utilise the institutional facilities.

ACKNOWLEDGEMENT

I would like to express my sincere gratitude to my beloved Professor and Director, Institute of Internal Medicine **Prof. P.Thirumalai Kolundu Subramaniam, MD,** for his guidance and encouragement.

This is one another fine moment to express my gratitude and indebtedness to by beloved Chief, **Prof. V.K. Rajamani, MD,** for his motivation, advice and valuable criticism, which enabled me to complete his work.

I am thankful to **Prof. V. Jeganathan, MD DM,** Head of the Department, Department of Cardiology, for allowing me to utilize the services of his department for the purpose of my study.

I should thank all the Assistant Professors in the Department of Cardiology for performing detailed Echocardiography for all the patients in the study.

I sincerely thank **Prof. Shameen Banu, MD,** Professor of Microbiology and all Assistant Professors in the Department of Microbiology for allowing me to utilise the laboratories services in their Department.

I am extremely thankful to the Medical Officers of Anti-Retroviral Clinic for helping me to perform the study.

I am extremely thankful to Assistant Professors of my parent unit, **Dr. G. Rajan MD,** and **Dr. S. Gopalakrishnan MD,** for their co-operation and guidance.

I am thankful to all my postgraduate colleagues for their constant support and sharp constructive criticism.

I should thank each and every patient for the whole hearted co-operation despite the morbidity they suffered.

I should thank each and every member of my family for the constant support and encouragement.

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INTRODUCTION

Human Immunodeficiency virus (HIV) belongs to the family Retroviridae and sub-family Lentivirinae. HIV-1 causes the Acquired Immunodeficiency Syndrome (AIDS). By definition, any HIV infected individual with a CD4 T cell count of less than 200/microliter has AIDS, regardless of the presence of symptoms or opportunistic diseases. AIDS was first recognized in the Unites States in 1981, when the US Centres for Disease Control and Prevention (CDC) reported the unexplained occurrence of Pneumocystis carinii (jirovecii) pneumonia in five previously healthy homosexual men in Los Angeles and of Kaposi's sarcoma in twenty-six previously healthy homosexual men in New York and Los Angeles. In 1983, Human Immunodeficiency virus was isolated from a patient with lymphadenopathy and in 1984 it was demonstrated clearly to be the causative agent of AIDS.

Early therapeutic goals focused on prolongation of life by aggressive treatment of often fatal opportunistic infections, such as Pneumocystis carinii (jirovecii) pneumonia. Descriptions of specific HIV related myocarditis and cardiomyopathy appeared during the 1980s and overall mortality fell with improved prophylactic regimens against opportunistic infection and clinical surveillance programmes. In the mid 1990s the advent of combination highly active antiretroviral therapy (HAART) made a major impact on the morbidity and mortality of HIV patients. Combination therapy reduces viral replication, delays disease

progression, and prolongs survival, while limiting development of viral resistance. Survival to 40-50 years is no loner unusual and coronary artery disease, either de novo or as an iatrogenic consequence of newer treatment regimens, is emerging as an important problem. Recent studies report increased rates of coronary events in HIV patients or in HIV patients receiving HAART.[40,41]Protease inhibitors, a main component of HAART, induce deleterious metabolic effects such as dyslipidemia and insulin resistance.[42]

HIV infection is characterized by an acquired, irreversible, profound immunosuppression that predisposes patients to multiple opportunistic infections, malignancies, and progressive dysfunction of multiple organ systems. HIV specifically infects and gradually depletes CD4+ lymphocytes but may also affect other cell types, including monocytes/macrophages, endothelial cells, glial cells, intestinal epithelial cells, and possible neurons. Studies have suggested that HIV may exhibit a cardiac tropism, but the heart may also be affected by other opportunistic viruses, fungi and protozoa. Cardiac disease associated with HIV may therefore be multi factorial, and can be caused by infectious or neoplastic complications or their treatments, any of the established causes of cardiac disease in other patient populations, or by HIV infection of the myocardium itself.[4] So, the knowledge of the relative frequency of each form of heart disease in patients with HIV is constantly evolving.

AIMS AND OBJECTIVES

- To find out the prevalence of cardiac disease in HIV positive individuals.
- To assess the correlation between the development of cardiac disease and the CD4 lymphocyte count in HIV positive individuals.
- To determine the correlation between clinical findings and echocardiographic cardiac involvement in HIV positive individuals.
- To know the common cardiac manifestations in the study group.

REVIEW OF LITERATURE

EPIDEMIOLOGY

The HIV pandemic enters its third decade and the resultant Acquired immunodeficiency syndrome (AIDS) is a global health crisis with approximately 36 million people affected worldwide. In 2004, the World Health Organisation estimated that there were 39.4 million people living with HIV/AIDS, 4.9 million new infections and 3.1 million deaths.[43] The cumulative death toll since epidemic began is over 20 million, the vast majority occurring in sub-Saharan Africa where over 13 million children have been orphaned. A total of 64% of all persons with HIV lives in sub – Saharan Africa with south Africa accounting for one third of the AIDS deaths globally. Since 2002, the steepest increase has been in East Asia (50%) attributable largely to the epidemic occurring in China and in Eastern Europe and Central Asia (40%). In Vietnam, Thailand, Cambodia, Nepal and Myanmar, HIV is now well established. In India, it is estimated that 5.1 million persons are currently infected; in Tamil Nadu 50% of the sex workers are infected and in Manipur over 5% of pregnant women are positive. In Northern India, HIV in well established in injection drug users, of whom 25 to 50% are infected. Given that Asia is home to 60% of world's population, these changes can have huge implications. The disease is now the principal cause of death in young adults in many parts of the USA and Europe.

The Mortality rate among patients with HIV infection has decreased markedly in the United States since the introduction of HAART. For example, in the HIV outpatient study, mortality among 1255 patients with at least CD4+ count <100 cells/mm^3 declined from 29.4 to 8.8 per 100 patient years between 1995 and the second quarter of 1997.[44] This decline coincided with the initiation of protease inhibitors for 80% of the study population. Similarly, in a European cohort study of 4270 patients who had had a CD4+ count < 500 cells/mm^3, mortality fell from 23.3 to 4.1 per 100 patient – years between mid-1995 and late 1997 to early 1998.[45] The decrease in mortality in these studies was accompanied by a decline the incidence of opportunistic infections[44] and correlated with the intensity of antiretroviral therapy.[45]

LITERATURE REVIEW

Cardiac involvement in AIDS was first reported in 1983 in a postmortem description of a 24 year old woman of Haitian origin with multiple complications of AIDS, including Kaposi's sarcoma involving the entire anterior cardiac wall without pericardial effusion.[8] Subsequently, cardiac involvement in patients with HIV infection has been described in multiple necropsies, clinical and echocardiographic series. Almost any agent that can cause disseminated infection in patients with AIDS may involve the myocardium, but clinical evidence of cardiac disease is usually overshadowed by manifestations in other organs, primarily the brain and lungs. Thus, the number of patients with AIDS

and cardiac involvement at necropsy greatly exceeds the number with significant cardiac disease during life. Estimates of prevalence vary widely from 28-73% [1] according to the screening methods elected. Although exact data are unavailable, conservative estimates derived from European and US series indicate cardiac morbidity and mortality in HIV patients of 6-10% and 1-9% respectively.[3, 4]

MYOCARDIAL DISEASE

The first case of rapidly fatal, dilated cardiomyopathy in a patient with AIDS was described in 1986. Among patients with dilated cardiomyopathy, HIV is the underlying cause in 4% [6], prognosis is poor and patients with HIV related cardiomyopathy have a mortality hazard ratio of 4.0 in comparison with controls with idiopathic dilated cardiomyopathy. Dilated cardiomyopathy affects 10-20% of those with HIV infection and accounts for approximately a third of HIV related deaths.[7] Median survival are 101 days in patients with left ventricular dysfunction compared with 472 days in HIV patients with a normal echocardiogram at the same stage of infection. Similarly, a longitudinal prospective study of HIV infected infants and children found that left ventricular dysfunction was a significant predictor of overall mortality, even after adjustment for age, height, CD4 cell count, and progressive neurological disease.[9]

Mechanisms

Dilated cardiomyopathy occurs late in the course of HIV infection and is usually associated with a significantly reduced CD4 count.[16] Pathological examination shows endocardial fibrosis and mural thrombus, particularly at the apex and histological evidence of myocyte hypertrophy and degeneration with increased interstitial and endocardial fibrillar collagen, often associated with evidence of previous myocarditis.The pathogenesis remains uncertain: speculated causes include direct infection of the heart by HIV itself, toxic effects of antiretroviral therapy, effects of circulating or systemic toxins, infection of the heart by opportunistic pathogens, toxicity of alcohol, illicit or self prescribed substances, and nutritional disorders.[36] Indeed, several of these factors may operate in an individual patient.

Direct correlation between histological cardiac abnormalities and clinical or functional heart muscle disease has not been established, making it difficult to determine whether cardiomyopathy is related directly to the presence of the virus or triggering of overt myocarditis.[21] In one prospective study of 952 asymptomatic HIV positive patients, an echocardiographic diagnosis of dilated cardiomyopathy was made in 76(8%) patients with a mean annual incidence of 15.9/1000 patients. All patients with echocardiographic abnormalities underwent myocardial biopsy; myocarditis was present in 63 (83%) of the patients with dilated cardiomyopathy and 36 (57%) of these had a positive hybridization signal

of HIV.[10] Co-infection with coxsackie virus, cytomegalovirus, and Epstein-Barr virus was also noted in may cases.[10] HIV virions may infect cardiac myocytes resulting in injury as a result of direct toxicity or activation of multifunctional cytokines (for example, endothelin-1, tumour necrosis factor-α, interleukin-6). The mode of entry of HIV into myocytes remains unclear since they are CD4 receptor negative. Further putative mechanisms of tissue damage include post viral autoimmunity and immune system dysregulation, adverse effects of viral proteins (including apoptosis), interference with β adrenergic stimulation, and transcriptional activation of cellular genes.

HIV infection may persist in reservoir cells within the myocardium and cerebral cortex despite anti-retroviral therapy and be associated with chronic release of cytotoxic cytokines. Thus, patients with encephalopathy have a higher likelihood of death from congestive heart failure than non encephalopathic controls (hazard ration 3.4).[17] Malnutrition and wasting are also important predictors of cardiac morbidity and mortality in HIV infection. There is a relation between trace element deficiency and cardiomyopathy, and the cardiac virulence of coxsackie virus is enhanced by selenium deficiency. Indeed, selenium supplementation has been shown to improve cardiac dysfunction in AIDS patients.[36]

Echocardiography [81] is helpful in the diagnosis of dilated cardiomyopathy and may also detect diastolic dysfunction in early

disease.[25,35] Computed tomography or magnetic resonance imaging may help to clarify the etiology, especially in cases secondary to neoplastic infiltration. The need for routine myocardial biopsy is controversial and associated risks are significant—sensitivity is low, especially in patchy lesions, and beyond research protocols its use is limited to patients with extensive cardiac damage with no identifiable cause.

Treatment for HIV related cardiomyopathy is generally similar to that for non-ischemic cardiomyopathy.[18] Angiotensin converting enzyme inhibitors and β blockers are recommended but may be poorly tolerated because of low systemic vascular resistance from diarrheal disease, infection or dehydration. Patients with myocarditis have enhanced sensitivity to digoxin and anticoagulation presents risks to patients with cerebral vasculopathy and possible aneurysm formation. The use of immunosuppressive regimens is controversial and no convincing benefits have been reported other than with intravenous immunoglobulin, [11] whose efficacy may reflect inhibition of cardiac auto antibodies by competition with Fc receptors or dampened effects of cytokines and cellular growth factors.

ENDOCARDIAL DISEASE

Three forms of endocarditis have been reported in HIV infected patients; marantic (non-bacterial thrombotic), bacterial and fungal.

Marantic endocarditis:

Marantic endocarditis can involve all four cardiac valves, though left sided lesions are more common. Vegetations are friable, consisting of platelets within a fibrin mesh with a few inflammatory cells, and systemic embolism is common. The condition, which is usually associated with hypercoagulable states in systemic lupus erythematosus, disseminated intravascular coagulation, and malignancy, is difficult to diagnose ante-mortem. Identification was frequent in early postmortem studies of patients with HIV infection, but the condition is now less commonly encountered, suggesting that its prevalence was overestimated in the past.

Bacterial endocarditis:

Bacterial endocarditis in HIV infection is infrequent, appearing almost exclusively in intravenous drug users where prevalence varies from 6.3-34%.[2] In North America, where most HIV affected patients are homosexuals, and endocarditis is uncommon. Intravenous drug users have frequent bacteraemias owing to the introduction of skin pathogens and talcum powder by unsterile intravenous injection. Vegetations form on the tricuspid and pulmonary valve with resultant pulmonary embolism and septic pulmonary infarction. Patients typically present with fever, sweats, weight loss, and co-existing pneumonia and/or meningitis. Infection affecting the left heart with systemic embolism is less common. Overall incidence of endocarditis in this group is falling; an unexpected

benefit of needle exchange and health education schemes,[26] and overdose is a more common cause of death. *Staphylococcus aureus* is the most common organism (>75%) followed by *Streptococcus pneumoniae* and *Haemophilus influenzae*, although these patients are also at increased risk of *Salmonella* infection. Methicillin resistant staphylococci have been reported, and the HACEK group of organisms (*Haemophilus influenzae, Haemophilus parainfluenzae, Actinobacillus actinomyceetemcomitans, Cardobacterium hominis, Eikenella corrodens, Kingella* species) should be considered in cases which are resistant to culture. Austrian's syndrome, characterized by acute streptococcal endocarditis, pneumococcal pneumonia, and meningitis, originally described in alcoholics, is also more common in AIDS patients.

Fungal endocarditis:

Fungal endocarditis is usually the result of systemic fungaemia. *Aspergillus* endocarditis has been reported in association with pulmonary aspergillosis, and cryptococcal and candidal endocarditis may complicate primary infection in the oropharynx and esophagus, particularly in patients nursed on intensive care units.

Excepting the late stage of AIDS, HIV infection appears to have little effect on susceptibility to or mortality from endocarditis, and aggressive treatment with conventional antibiotic regimens and surgery when required are appropriate. Medical treatment is successful in > 70%

of cases and surgery also has good outcome, provided that intravenous drug abuse does not resume in the postoperative period.

PERICARDIAL DISEASE

Pericardial disease is a frequent cardiovascular manifestation of HIV infection often associated with shortened survival, independent of CD4 count and albumin values.[6,27] The prevalence of pericardial disease at echocardiography ranges from 10-59% and was 21% in the largest series of 1139 patients.[27] In Africa and many US urban settings, pericardial effusion associated with HIV is now the most frequent cause of pericardial disease. The clinical spectrum includes effusions with and without cardiac tamponade, constrictive pericarditis and neoplastic infiltration by lymphoma and Kaposi's sarcoma.[39] There is no apparent correlation between clinical stage of HIV infection and severity of pericardial involvement.

Pericarditis is usually non-specific in origin and can occur with or without effusion. Initial symptoms and signs may be subtle but include chest pain and signs of tamponade and hypotension. Low pressure tamponade may be encountered in patients with AIDS who are severely dehydrated and cachectic with low resting right ventricular filling pressures. The cause of pericardial effusion is frequently difficult to determine though it may be associated with Kaposi's sarcoma, lymphoma, and bacterial [38] (*Mycobacterium* species, *Nocardia* species, *Staphylococcus aureus*), viral (herpes simplex, cytomegalovirus virus),

and fungal (*Cryptococcus neoformans*) infection. In one typical series of 66 HIV patients with cardiac tamponade, 26% were caused by tuberculosis, 17% were purulent, 8% were caused by atypical mycobacteria, and 10% by Kaposi's sarcoma and lymphoma. HIV itself has been isolated from macrophages within the pericardial fluid of one patient, though its role remains uncertain. Culture of pericardial fluid is often unrevealing and effusion may be part of generalized serous effusive process also involving pleural and peritoneal surfaces, possibly related to enhanced expression of cytokines (for example, tumour necrosis factor α) in the later stages of HIV disease.[6]

Small asymptomatic effusions do not require diagnostic evaluation and spontaneously resolve in up to 42% of patients.[6] Tuberculosis in AIDS is often atypical with a high prevalence of extra pulmonary manifestations, and in areas such as Africa where the incidence of tuberculous infection is high, patients with pericardial effusion often receive empirical anti tuberculous chemotherapy. Pericardiocentesis is currently recommended for patients with large or poorly tolerated effusions, diagnostic assessment in the presence of systemic illness, or cardiac tamponade. The effect of HAART on pericardial effusion is unknown.

MALIGNANT DISEASE

Two types of malignancy affect the heart in HIV patients: Kaposi's sarcoma, and malignant lymphoma, of which the former is more common.

Kaposi's sarcoma:

Kaposi's sarcoma is a low grade neoplasm arising from mesenchymal or endothelial cells and occurs in approximately 30% of AIDS patients, mostly male homosexuals. Cardiac involvement usually reflects a widely disseminated process.[8] Visceral and parietal pericardial lesions are most common though involvement of the myocardium, coronary arterial adventitia, great vessels, epicardium, and epicardial fat has also been described. Nodular coalescent dark red or violaceous plaques are characteristic and histological examination reveals nodular lesions formed by spindle cells surrounding slit-like capillary vessels. Cardiac Kaposi's sarcoma is usually occult and rarely diagnosed during life. Pericardial involvement may rarely manifest as tamponade or constriction and underlying myocardial function is rarely affected.[39]

Malignant Lymphoma:

The frequency of non-Hodgkin's lymphoma in patients with AIDS is increasing and estimated to be 25-60 times greater than expected in the general population. Lymphomas are observed in 5-10% of patients infected with HIV and constitute the first manifestation of AIDS in 3-4%

of new cases.[28] Most non-Hodgkin's lymphomas affecting the heart in HIV infection are high grade, with Burkitt-like cells, reticular cell sarcomas, or large cell immunoblastic sarcomas. The majority originates from B cells and display monoclonal immunoglobulin staining. Pathological examination demonstrates pallor of the heart secondary to diffuse lymphomatous infiltration or patchy involvement of the epicardium, myocardium, and endocardium in the form of focal circumscribed nodules, most frequently affecting the right atrium. Histological sections contain infiltrates of plasmacytoid lymphocytic cells, resembling immunoblastic non-Hodgkin's lymphoma, and evidence of intense mitotic activity. Extra-nodal sites of lymphoma (typically the central nervous system, gastrointestinal tract and bone marrow) are common and metastatic cardiac involvement may reflect this dissemination. Secondary cardiac involvement may also arise by direct extension of mediastinal mass through the pericardium. Primary cardiac lymphoma is extremely rare but has been reported in patients with HIV.

Clinical manifestations of cardiac lymphoma include cardiomegaly, pericardial effusion, congestive heart failure, arrhythmias or progressive heart block. Sudden death is rare and most patients have no evidence of cardiac dysfunction. Outcome is usually poor and the optimal approach to treatment has yet to be determined, though clinical remission has been obtained with combination chemotherapy.[28]

DRUGS AND CARDIOTOXICITY

Until recently, the prognosis of AIDS was so poor that concerns about long term effects of drug treatment were minor. The advent of potent antiretroviral drugs has had an impressive effect on mortality, disease progression, and incidence of HIV related disorders. Indeed, HIV infection should be considered a chronic condition in an increasing proportion of patients, and issues relating to long term drug treatment are of increasing relevance.[29]

CORONARY DISEASE

In 1998, severe premature coronary disease was first reported in 2 young men with HIV infection receiving HAART, specifically Protease inhibitors.[46] In a retrospective database study of 36766 HIV patients treated at Veterans Affairs facilities between 1993 and 2001, no increase in cardiovascular or cerebrovascular events was observed during a mean follow up of 40 months among patients receiving HAART.[47] Similarly in a meta analysis of 30 randomized clinical trials, the incidence of myocardial infarction (MI) was not higher in patients receiving protease inhibitors compared with nucleoside reverse-transcriptase inhibitors ; however, the duration of treatment was only 1 year, and the number of events was small.[48]

On the other hand, in the HIV outpatient Study, myocardial infarction (MI) occurred in 19 of 3247 patients taking but in only 2 of

2425 not taking Protease inhibitors, and the frequency of MI increased after the introduction of these drugs (P=0.0125).[40] The Data Collection on Adverse Events of Anti- HIV Drugs Study Group prospectively followed up 23468 HIV patients for a mean of 1.6 years, with an average exposure to antiretroviral therapy of 1.9 years. The risk of MI increased with longer exposure to combination antiretroviral therapy; the adjusted relative rate per year of exposure was 1.26. In a study of 1551 Italian HIV patients followed up for a median of 36 months, 25 coronary events (MI in 13 and unstable angina in 12) were diagnosed[49]. The cumulative annual incidence of coronary events was 9.8 per 1000 patients in those treated with Protease inhibitors compared with 0.4 per 1000 in those not treated.

Taken together, these studies suggest that he rate of myocardial infarction is higher in HIV patients taking Protease inhibitors and that the risk increases as the duration of treatment lengthens.[20] The classic coronary risk factors usually exert their influence for decades before a coronary event occurs. That an increase in risk can detected after a much shorter exposure to Protease inhibitors suggests either that they are a potent atherogenic stimulus or that their use is associated with a period of high risk. The coronary event rates on these studies are relatively low but might be expected to be higher as the HIV population ages.

Clinical Features

Compared with HIV- uninfected patients, the mean or median age of the patients was very young, ranging from a mean or median of 42 to

50 years. This was 5 years older than other HIV patients in the French cohort study[51] and 11 years younger than control non-HIV patients with acute coronary syndromes in our study.[52] More than half of the patients in each of these studies smoked cigarettes at the time of their coronary event. The proportion of patients receiving Protease Inhibitors ranged from 49% to 71%.

Mean HDL cholesterol levels were very low in each of the 3 studies in which they were reported: 32±10 mg/dl, [50] 28±10 mg/dl,[51] and 32±12 mg/dl.[52]

These levels were significantly lower than those of HIV patients without coronary disease in the French cohort[51] and lower than non-HIV control subjects with coronary disease in the other two studies. [50,52] Mean LDL cholesterol levels were lower in HIV coronary patients than in non-HIV coronary subjects in one study[50] but not another.[52] In the French cohort, LDL cholesterol levels were much higher in the HIV patients than in those without coronary disease.[51]

Thus, the typical HIV patient with coronary disease is a male smoker with very low HDL cholesterol levels who is significantly younger than HIV – uninfected patients with coronary disease. Coronary angioplasty or stenting has often been performed in these patients, and the immediate results have been excellent; however. The restenosis rate appears to be much higher than that of patients without HIV infection.[50, 52] Atherosclerosis might develop more rapidly in venous bypass grafts in

HIV patients because it appears to progress more rapidly in native arteries.[52]

Cardiomyopathy

Zidovudine was the first widely available antiretroviral drug and is still used in pregnant mothers who are HIV positive (and their newborns) and in combination regimens. Drug induced dilated cardiomyopathy secondary to mitochondrial toxicity has been associated with its use in adults and children.

Dyslipidaemia and cardiovascular risk:

Hyperlipidaemia, hyperglycaemia, hyperinsulinaemia, and lipodystropy are frequent adverse effect of potent antiretroviral combination therapy, particularly involving protease inhibitors.[30] Hyperlipidaemia affects approximately 50% of patients using protease inhibitors, with average increases in total cholesterol and triglyceride concentrations of 28% and 96% respectively. The degree of increase seems to be proportional to the duration of treatment and type of drug.

ATHEROSCLEROSIS IN HIV

There are several possible explanations for the increase in coronary events in HIV patients. Protease inhibitors induce deleterious metabolic effects such as dyslipidemia and insulin resistance.[42] An alternative possibility is that HIV disease is in itself atherogenic. Progressive HIV

disease is associated with accelerated T-cell proliferation, heightened T-cell activation, and high levels of inflammatory markers. [61, 62]. These immunological perturbations persist even after the introduction of HAART.[63] Indeed, persistent levels of immune activation are observed even after years of treatment mediated viral suppression. The level of immune activation has been independently associated with CD4 T-cell nadir,[64] which was a predictor of progression of Carotid Intima Media Thickness.

Both immunodeficiency and immune reconstitution may be atherogenic. T lymphocytes, of which CD4 cells constitute the major population, play a key role in atherogenesis.[65, 66] CD4 cell activation promotes atherosclerosis through elaboration of proinflammatory cytokines, including tumour necrosis factor and interleukins[67]. Analogously, T-cell lymphocytes are also involved in the arteriosclerosis that develops in immune – suppressed patients after cardiac transplantation.[68]

Chronic low – grade inflammation contributes to accelerated atherosclerosis.[69] C- reactive protein levels are higher in HIV patients than in control subjects, and subjects with levels of this marker in the upper quartile or quintile have an elevated risk of cardiovascular events.[70] Some experimental data indicate that C-reactive protein is an active participant in the process of atherogenesis.[71,72]

Monocyte chemoattractant protein -- 1 is a potent activator of macrophages and monocytes, stimulating them to migrate to the sub endothelial space where they begin phagocytosis of modified lipoproteins to become lipid-laden foam cells, an early step in atherogenesis. Among HIV patients with sub clinical atherosclerosis by carotid and femoral ultrasound, monocyte chemo attractant protein-1 plasma levels were higher and the frequency of a mutation in the promoter region of the monocyte chemo attractant protein-1 gene was also higher compared with HIV patients without atherosclerosis.

Coagulation abnormalities that would predispose to thrombotic event have been described in HIV patients.[73] Protein S deficiency is the most common, reported in 73% of HIV infected men in a study.[74] Serum levels of von Willebrand factor are higher in untreated HIV patients than in control subjects, reflecting endothelial activation, but tend to decrease toward normal with HAART.[75] Platelet activation is also enhanced in HIV patients.[56] Platelet activation is also enhanced in HIV patient.[75] Smoking cigarettes activates platelets and increases coagulability, and smoking rates are very high in HIV patients. Endothelial dysfunction[13], inflammation, platelet activation and hypercoagulability interact synergistically to enhance the atherogenic and thrombotic milieu of the arterial wall.

ENDOTHELIAL DYSFUNCTION IN HIV

HIV can damage endothelium through several mechanisms. Tat protein, a small cationic polypeptide that can be released from infected cells, interacts with at least 3 different types of receptors present on the surface of endothelial cells.[15,57] The resultant activation of several signal transduction pathways triggers the expression of adhesion molecules, vascular endothelial growth factor, and platelet activating factor.[57] As a consequence, Tat protein causes endothelial dysfunction.[58] The death of CD4 T lymphocytes caused by HIV results in an increase in shed membrane particles from these cells.[59] Shed membrane particles from T lymphocytes induce endothelial dysfunction, expressed as reduction in nitric oxide and prostacylin-induced vasodilation.[60]

ENDOTHELIAL DYSFUNCTION AND HAART

Endothelial dysfunction is a feature of early atherosclerosis and a predictor of future cardiovascular events.[14,15] HIV infected children have endothelial dysfunction compared with age and sex matched control subjects in the absence of cardiovascular risk factors.[54] The use of Protease inhibitors in HIV infected adults is associated with endothelial dysfunction as assessed by brachial artery flow mediated vasodilation.[55] This abnormality appears to be mediated by the atherogenic dyslipidemia induced by Protease inhibitors.[55]

Soluble adhesion molecules indicative of endothelial damage are elevated in HIV infected patients.[56] In another study, patient receiving HAART had higher levels of P-selectin. Plasminogen activator inhibitor type 1, and tissue plasminogen activator but not soluble intracellular adhesion molecule-1, and there was no significant difference in the levels of these markers between patients receiving Protease inhibitors and non-Nucleoside reverse transcriptase inhibitors.

Preliminary guidelines for the evaluation and management of dyslipidaemia in HIV positive patients receiving HAART have recently been published.[31] Key points are routine screening, lifestyle advice (including smoking cessation) and comprehensive lipid analysis before commencing antiretroviral therapy, and treatment of selected cases. Statins which are independent of the cytochrome P450 system (for example, pravastatin, atorvastatin) are recommended to avoid interaction with protease inhibitors, and use of fibrates and gemfibrozil has been described in patients with isolated hypertriglyceridaemia.

In some patients, with high atherosclerotic co-morbidity or risk, a high CD4+ cell count, and low viral load, the risk: benefit ration of treatment with HAART may be questionable.

PULMONARY HYPERTENSION

Primary pulmonary hypertension has been reported in HIV infected patients without evidence of thromboembolic disease, intravenous drug

use, right sided endocarditis or pulmonary infection. Development and progression bear no relation to the stage of underlying HIV disease. It affects about 0.5% of hospitalized AIDS patients and is a cause of severe cardiac impairment with associated cor pulmonale and death.[6] Histological examination most frequently demonstrates plexogenic pulmonary arteriopathy. The pathogenesis is multifactorial and an intriguing puzzle: HIV may cause endothelial damage and vasoconstriction through release of endothelin-1, interleukin-6, and tumor necrosis factor α, oxide anions, and proteolytic enzymes in response to infection.[24] Therapeutic effects of oxygen, steroids, calcium channel blockers, epoprostenol, and nitric oxide have all been proposed though efficacy has not been confirmed in controlled clinical trials.[33] Effects of HAART on pulmonary artery endothelial cells are unknown.

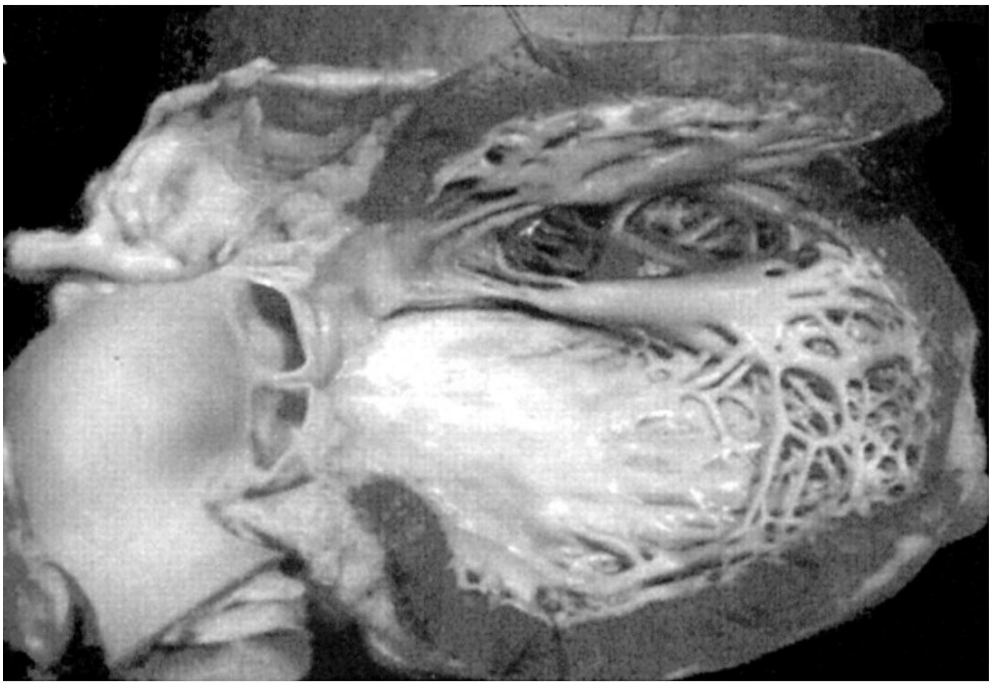
The effect of antiretroviral treatment on pulmonary hypertension is not known. However, in a recent report from the Swiss Cohort study, pulmonary artery pressure increased in untreated patients but decreased in patients treated with HAART.[79] The oral endothelin receptor antagonist bosentan improved exercise tolerance and hemodynamic measurements in a small study of HIV patients.[80]

With current advances in HIV/AIDS management and increased survival, cardiac manifestations of HIV disease will become more important and encountered more frequently. HAART is only available to a minority of HIV infected individuals worldwide and studies from the

pre-HAART period still apply. Risk factors for vascular disease should be monitored in patients receiving HAART.[23]

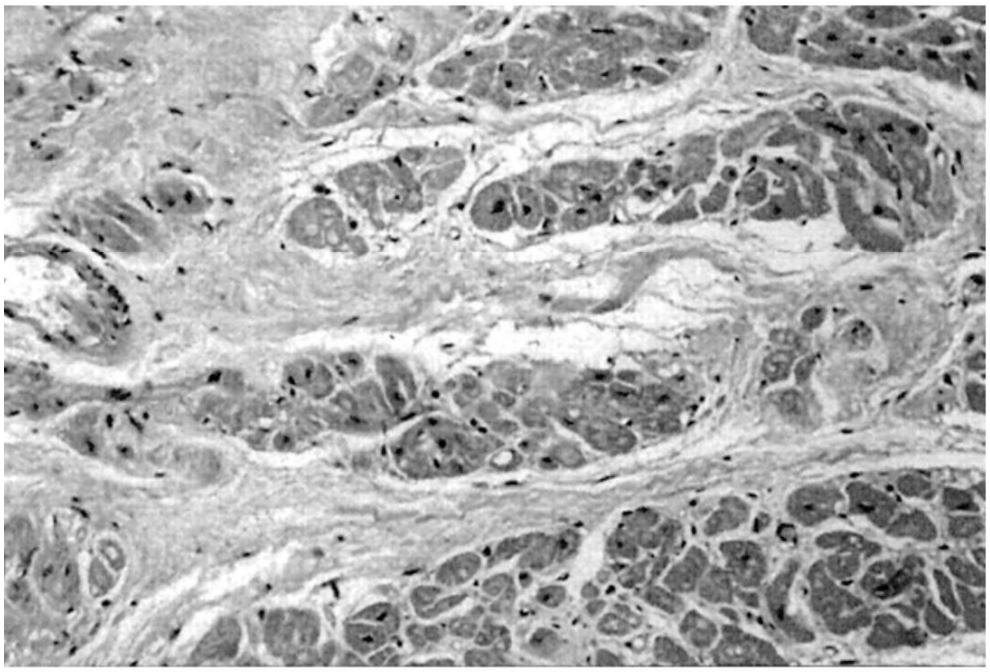
The heart may be a marker of the HIV infected patient's overall health, and a decline in cardiac function should trigger more comprehensive evaluation. As the role of infection and inflammation in many other cardiovascular diseases is now recognized, identification of the molecular mechanisms of HIV related heart disease may have broader implications for a wide range of patients.

DILATED CARDIOMYOPATHY IN AIDS PATIENT



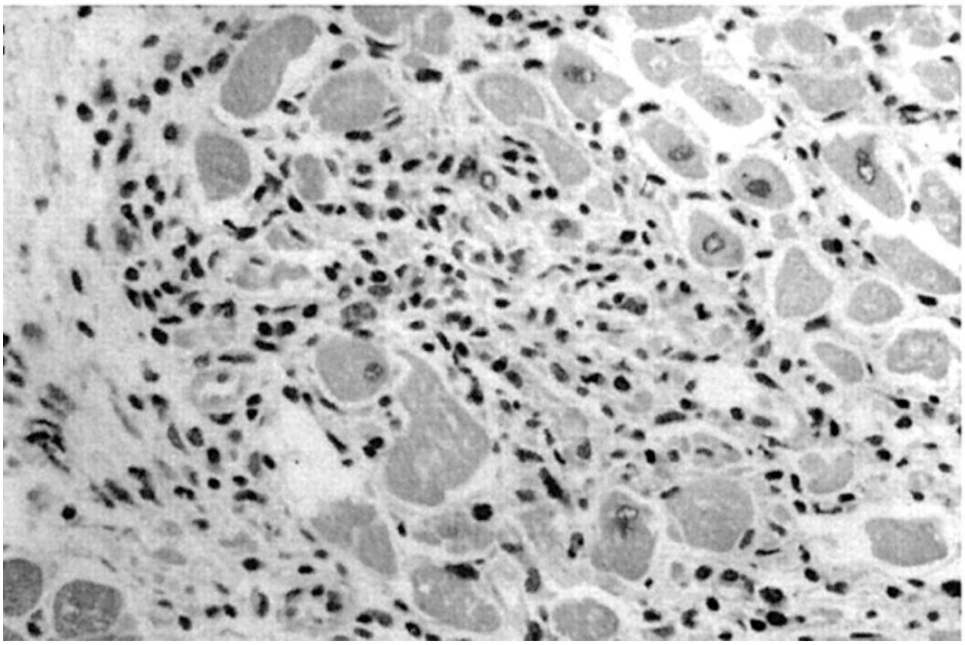
The heart has globular shape with rounded apex due to ventricular dilation. The LV cavity is enlarged with mild myocardial hypertrophy. There is diffuse endocardial fibrous thickening

DILATED CARDIOMYOPATHY IN AIDS PATIENT



Histological examination reveals myocyte hypertrophy with increased interstitial collagen

DILATED CARDIOMYOPATHY IN AIDS PATIENT



Histological examination reveals evidence of myocarditis with lymphocytic infiltrate and myocyte necrosis.

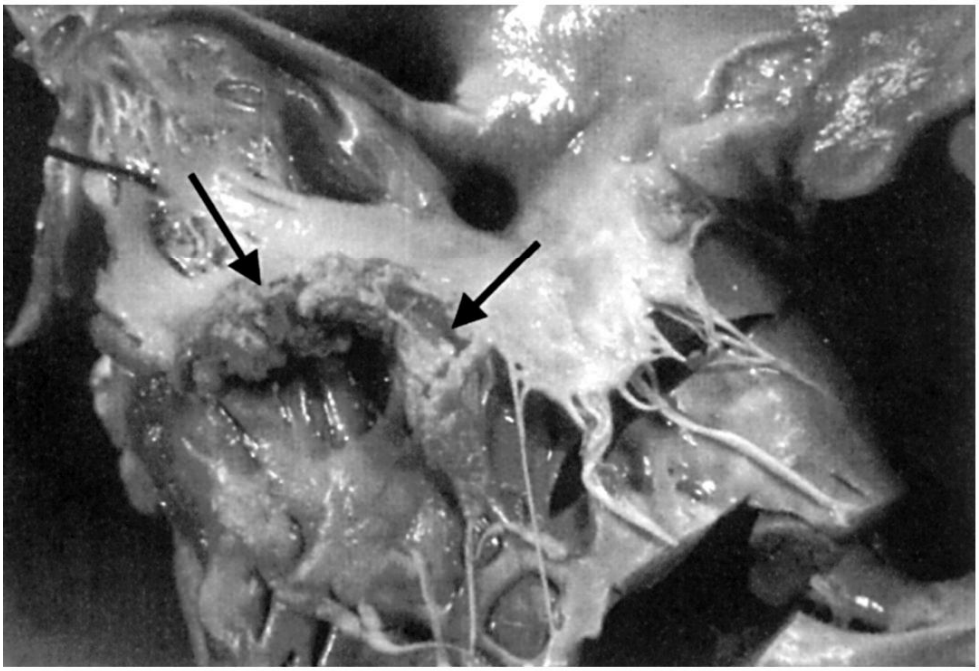
PERICARDITIS

Fibrinous pericarditis in AIDS patient induced by Myocobacterium avium complex.

CARDIAC KAPOSI'S SARCOMA IN AIDS PATIENT

Epicardial lesions appear as coalescent plaques.

ENDOCARDITIS OF TRICUSPID VALVE



Large polypoid thrombotic lesion is seen on posterior leaflet of Tricuspid valve in iv drug abuser with AIDS.

MATERIALS AND METHODS

The study was performed in the Institute of Internal Medicine, Government General Hospital in close association with the Department of Cardiology and the Department of Microbiology in the same hospital.

The study is an observational type of study. Forty five patients who were detected to be HIV positive were included in the study. The patients were selected from the inpatient wards of the Institute of Internal Medicine, Government General Hospital.

The HIV serology of the study population was done by double Enzyme Linked Immuno-Sorbent Assay (ELISA) using Microwell ELISA test at the Department of Microbiology, Government General Hospital. If the ELISA was positive initially, it was repeated twice to confirm the HIV seropositive state.

All patients were:-

- Questioned for the symptoms suggestive of cardiac illness i.e. chest pain, palpitations, shortness of breath, syncope, swelling of lower limbs, abdominal distention and decreased urine output. The duration of each symptom was noted.

- Questioned on the history regarding sexual exposures, abuse of intravenous drugs, prior blood transfusions, occupation and marital status.

- Subjected to detailed and complete general examination for the presence of anemia, cyanosis, clubbing, icterus, generalized lymphadenopathy and pedal edema. The pulse, respiration and blood pressure were recorded. A thorough cardiac examination which included the jugular venous pressure and waveforms, apical impulse, presence of thrill and palpable sounds, the intensity of heart sounds, presence of added sounds and murmurs was carried out. The respiratory system, central nervous system and abdomen were also examined.

Complete blood count, blood urea, sugar, serum creatinine, liver function tests, urine routine analysis and ultrasonography of the abdomen and pelvis were done for all patients. Fasting serum lipid profile was done for patients above the age of forty year. The CD4 lymphocyte count was done at the Department of Microbiology by Flow Cytometry method (FACS count equipment, manufactured by B.D.).

An erect chest x-ray (postero-anterior view) on deep inspiration was taken and analyzed for cardiomegaly, pleural effusions, pulmonary hypertension and pulmonary edema. Chest X-rays were taken using 100mA x-ray machines manufactured by G.E. at the Barnard Institute of Radiology, Government General Hospital

A standard twelve lead resting electro-cardiogram was done for all patients in the Department of Cardiology using Philips ECG machine. The various aspects of the P wave and the QRS complexes, ST-T changes

and other electro-cardiographic features suggestive of pericarditis, myocarditis, pericardial effusion, pulmonary hypertension and left ventricular dilatation were noted.

Two dimensional echocardiography with colour flow Doppler was done for all patients in the study at the Department of Cardiology using Aloka Equipment. Echocardiogram was done to evaluate the presence of pericardial effusion, chamber dilatation, myocardial dysfunction, ejection fraction, pulmonary hypertension and valvular lesions.

INCLUSION CRITERIA

HIV seropositive patients; seropositivity being confirmed by ELISA at the Department of Microbiology, Government General Hospital, Chennai.

EXCLUSION CRITERIA

- Patients on treatment with Highly Active Anti-retroviral Therapy (HAART).
- Patients with Hyperlipidemia, Systemic Hypertension, Diabetes Mellitus, Ischemic Heart Disease, Rheumatic Heart Disease, Congenital Heart Disease and Collagen Vascular Disorders.

OBSERVATION

The study group included 45 patients. There were 37 (82%) male and 8 (18%) female patients. The study patients fell into the age group between 24 and 45 years.

Of the 45 patients, 22 patients had symptoms referable to the cardio-vascular system. This amounted to 49% of total patients. The common symptoms in decreasing order of frequently are given in the table below:-

Sl.No.	SYMPTOMS	No. OF PATIENTS
01	Shortness of Breath	17
02	Chest Pain	08
03	Swelling of Lower Limbs	08
04	Palpitations	07
05	Decreased Urine Output	06

General examination and clinical examination with relevance to cardiac system revealed the following signs as in the table given below:-

General Examination

Sl.No.	SIGNS	No. OF PATIENTS
01	Oropharyngeal Candidiasis	15
02	Tachypnea	14
03	Generalised Lymphadenopathy	11
04	Pedal Edema	09
05	Pallor	05
06	Cyanosis	-
07	Icterus	-
08	Clubbing	-

Cardiac Examination

Sl.No.	SIGNS	No. OF PATIENTS
01	Tachycardia	18
02	Elevated JVP	09
03	Systolic murmur in apex	03
04	Third Heart Sound	03
05	Pericardial Rub	03
06	Loud P2	01

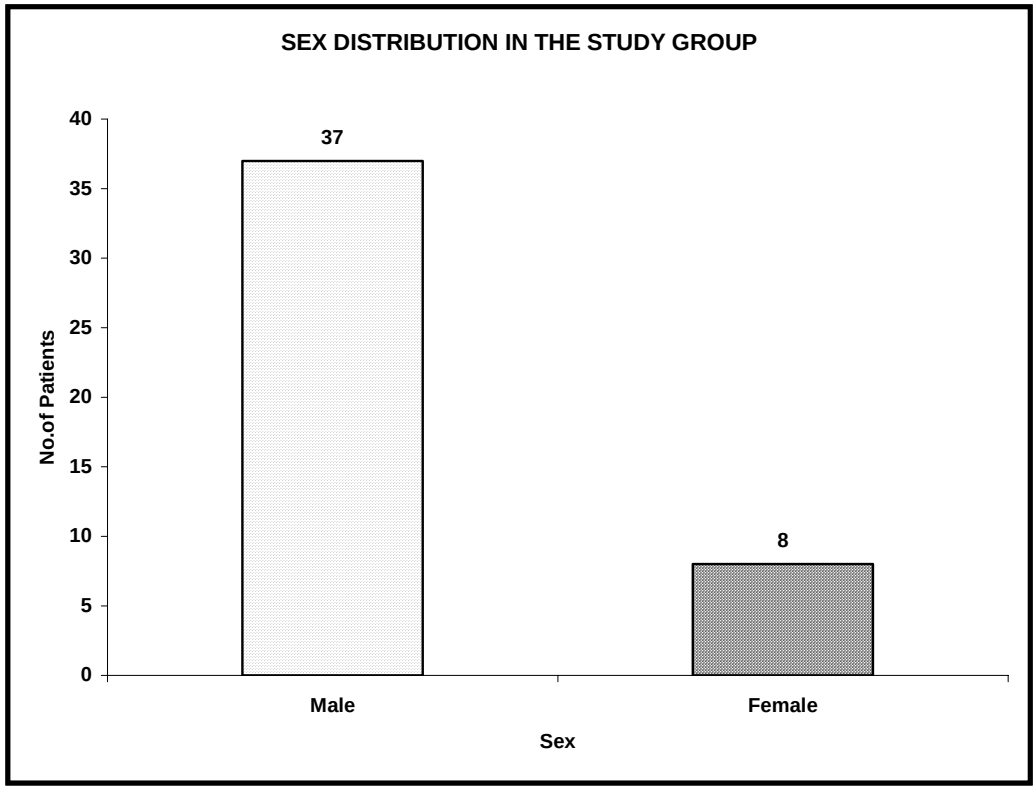
The most common ECG change observed was Sinus Tachycardia seen in 18(40%) patients. Sinus Tachycardia was not only due to cardiac disease but also associated conditions like pulmonary diseases, fever, anemia, etc. The ECG changes observed are given in the table below:-

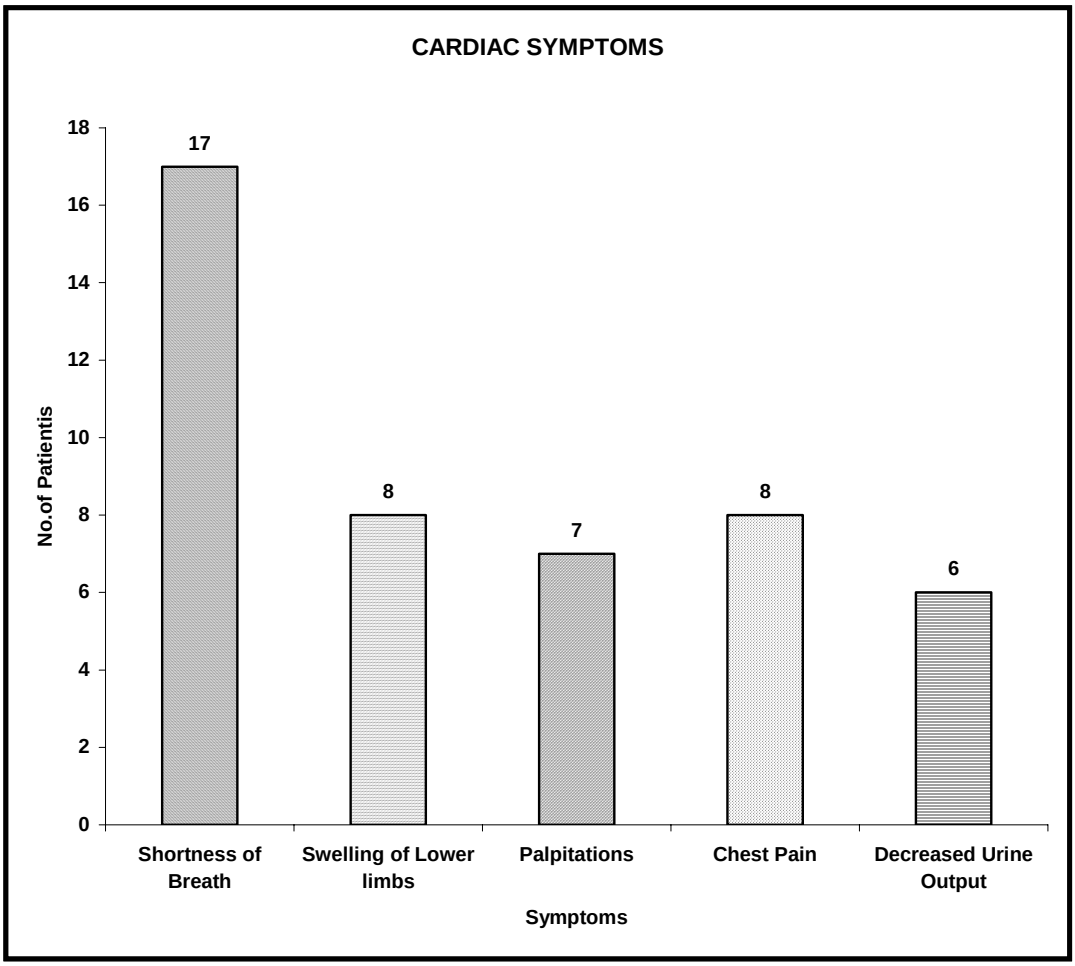
Sl.No.	ECG FINDINGS	No. OF PATIENTS
01	Sinus Tachycardia	18
02	Low Voltage complexes	04
03	Diffuse ST-T changes	02
04	P Pulmonale	01
05	Right Axis Deviation	01
06	Right Ventricular Hypertrophy	01

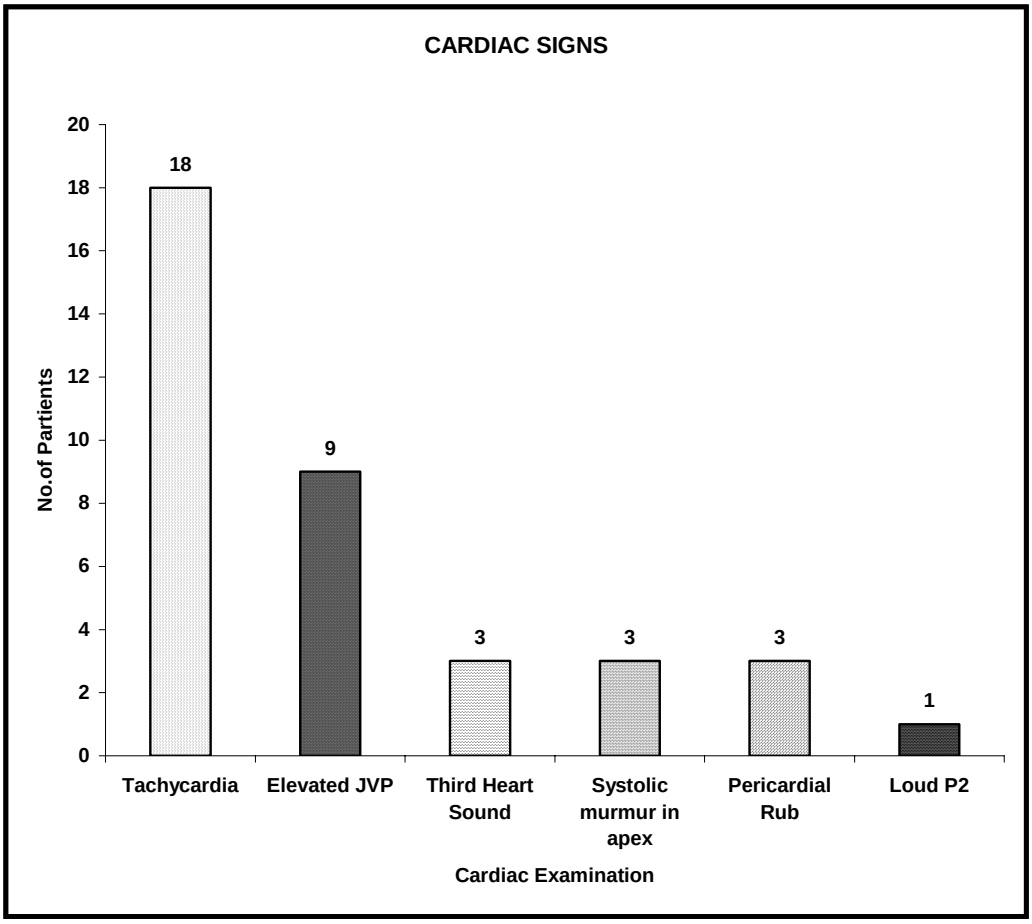
Echocardiogram abnormalities were seen in 12 patients who accounted for 27% of the total patients. The Echocardiographic changes in decreasing order of occurrence are given in the table below:-

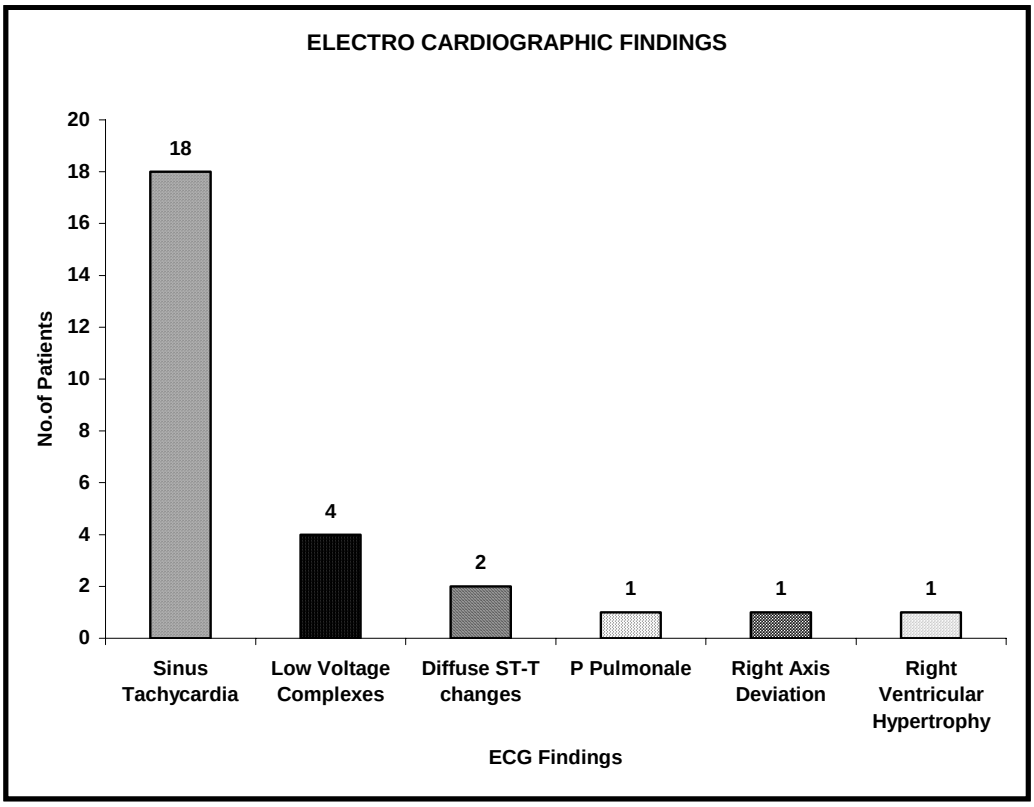
Sl.No.	ECHO FINDINGS	No. OF PATIENTS
01	Pericardial Effusion	6
02	Dilated Cardiomyopathy	2
03	Mild Left Ventricular Dysfunction	2
04	Pulmonary Hypertension	1
05	Vegetations over Tricuspid Valve	1

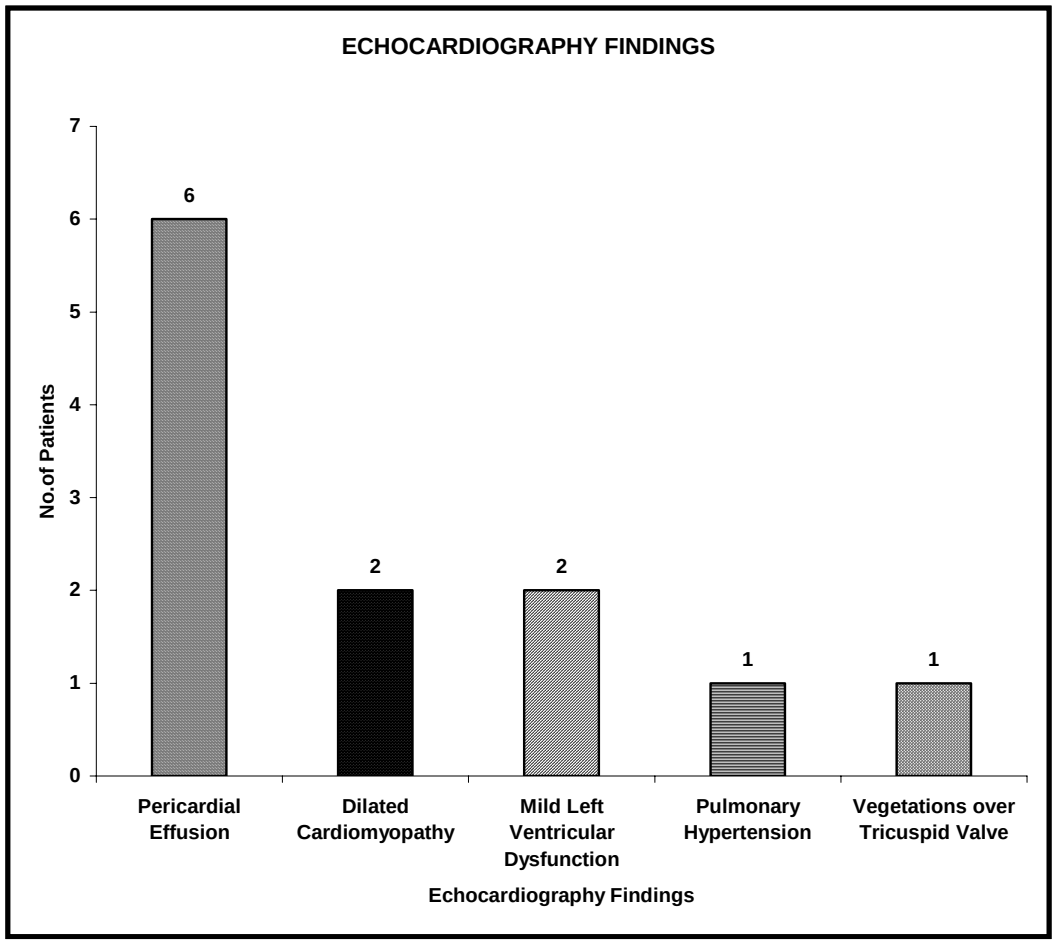
Nine out of twelve patients with echocardiographically demonstrable cardiac lesions had HIV disease for more than 18 months duration. All the twelve patients with cardiac lesions echocardiographically had CD4 lymphocyte count of less than 250 cells/mm^3.

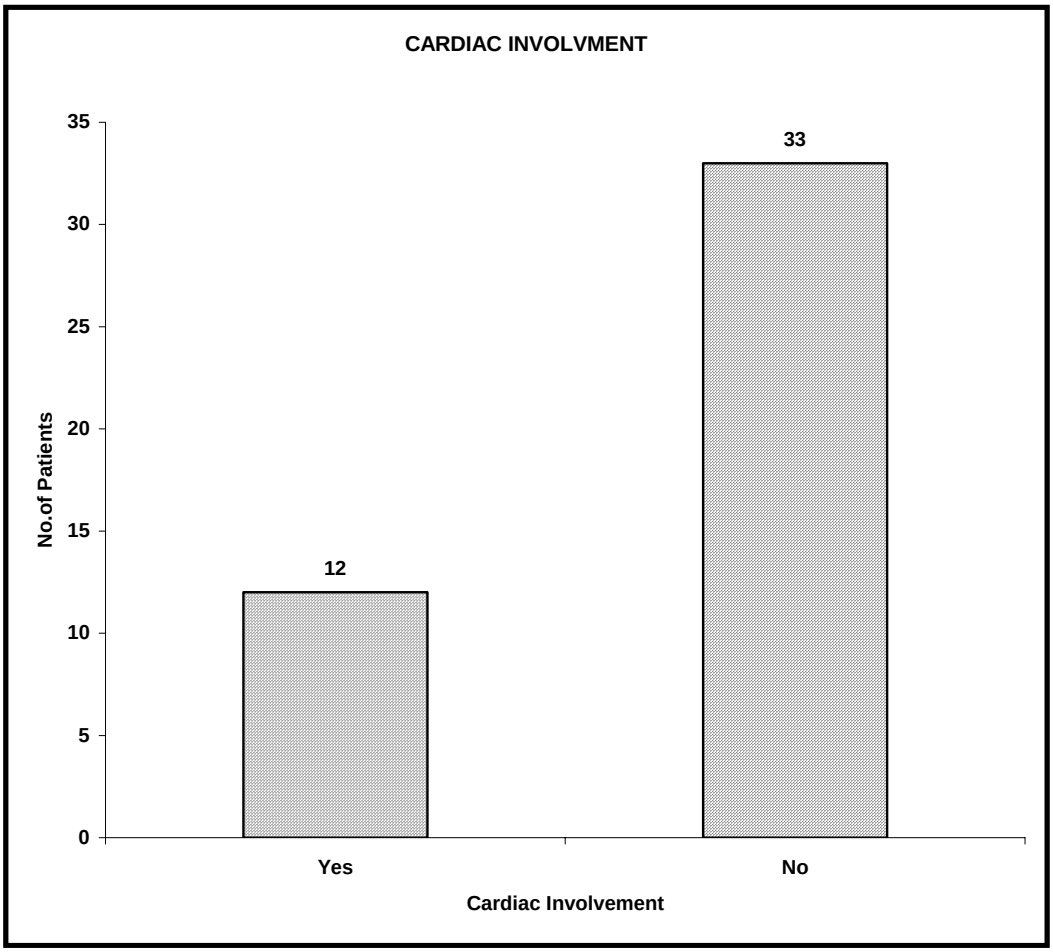

SEX DISTRIBUTION IN THE STUDY GROUP
No.of Patients
40
35
30
25
20
15
10
5
0
37
8
Male
Female
Sex


CARDIAC SYMPTOMS
No.of Patientis
18
16
14
12
10
8
6
4
2
0
17
8
7
8
6
Shortness of Breath
Swelling of Lower limbs
Palpitations
Chest Pain
Decreased Urine Output
Symptoms

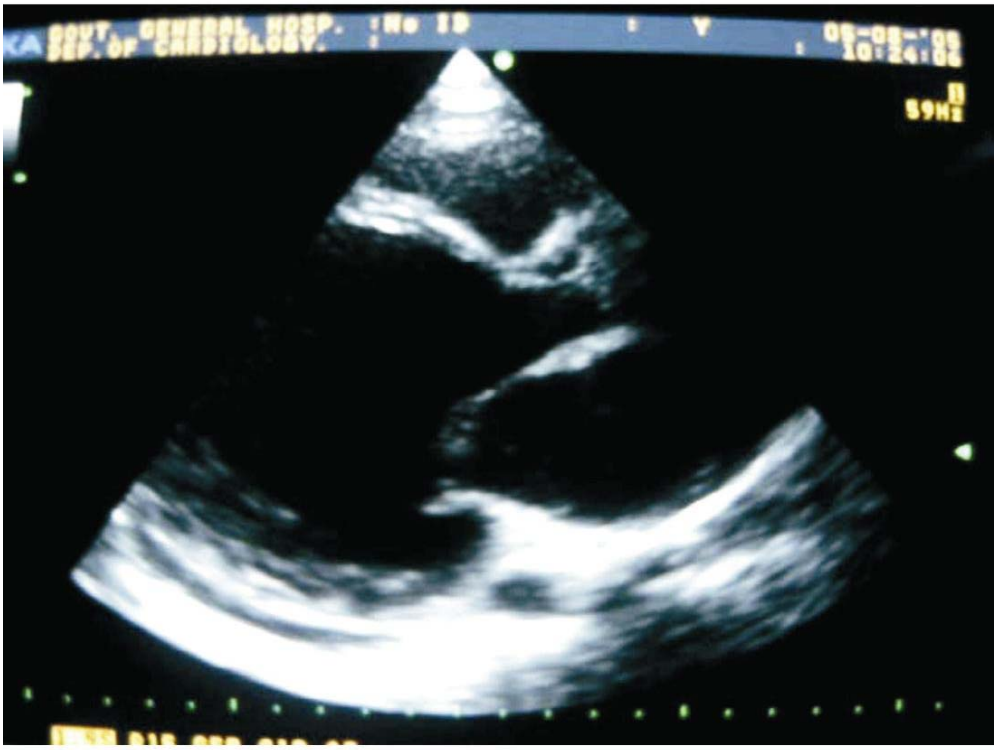

CARDIAC SIGNS
No.of Partients
20
18
16
14
12
10
8
6
4
2
0
18
9
3
3
3
1
Tachycardia
Elevated JVP
Third Heart Sound
Systolic murmur in apex
Pericardial Rub
Loud P2
Cardiac Examination


ELECTRO CARDIOGRAPHIC FINDINGS
No.of Patients
20
18
16
14
12
10
8
6
4
2
0
18
4
2
1
1
1
Sinus Tachycardia
Low Voltage Complexes
Diffuse ST-T changes
P Pulmonale
Right Axis Deviation
Right Ventricular Hypertrophy
ECG Findings


ECHOCARDIOGRAPHY FINDINGS
No.of Patients
0
1
2
3
4
5
6
7
6
2
2
1
1
Pericardial Effusion
Dilated Cardiomyopathy
Mild Left Ventricular Dysfunction
Pulmonary Hypertension
Vegetations over Tricuspid Valve
Echocardiography Findings

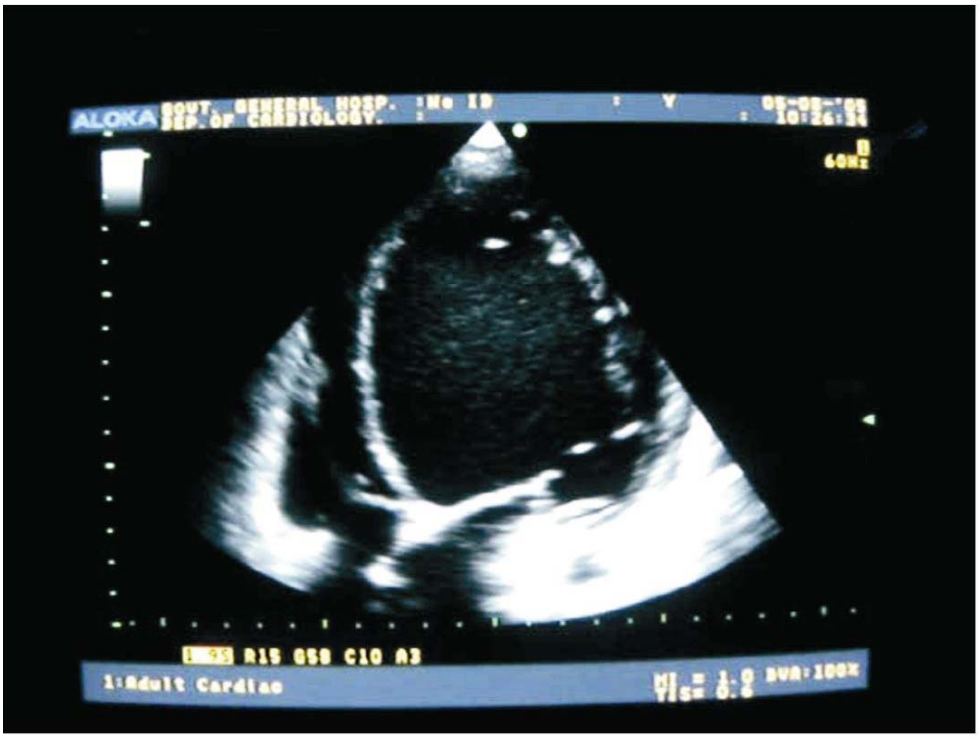

CARDIAC INVOLVMENT
35
30
25
20
15
10
5
0
No.of Patients
12
33
Yes
No
Cardiac Involvement

ECHOCARDIOGRAM OF A HIV PATIENT WITH DILATED CARDIOMYOPATHY



Parasternal long axis view

ECHOCARDIOGRAM OF A HIV PATIENT WITH DILATED CARDIOMYOPATHY



Apical four chamber view

DISCUSSION

Cardiac manifestations of HIV infection have not attracted much attention because the clinical picture of HIV infection is still dominated by opportunistic infections and malignancies. In this study, 12 patients (27%) had some form of cardiac involvement.

Symptom Analysis:

In this study, 22 (49%) patients had symptoms referable to cardio vascular disease, in the form of breathlessness, palpitations, chest pain, swelling of lower limbs, and decreased urine output. Of this breathlessness was the most common symptom encountered in 38% of the patients followed by chest pain in 18% of the patients. Although breathlessness and chest pain were considered in the symptoms of cardiac disease, their clinical implications must be taken with a degree of caution, as they could be attributable to pulmonary and pleural diseases and anemia of chronic disease in HIV infection as shown in the study by Nzuobontane et al.[32]

Pericardial Disease:

Pericardial disease was observed in 6 (13%) patients in the study. In 3 patients, there was only minimal pericardial effusion and these patients were followed up. Repeat echocardiogram after three months showed complete resolution of the pericardial effusion in 2 of these

patients and in the third patient the effusion completely resolved after five months by echocardiogram. Studies done by Jose Silva-Cardoso et al [34] showed that 41% of the patients had minimal asymptomatic pericardial effusion, 13% had moderate to severe pericardial effusion and 0.55% had acute pericarditis.

One patient with severe pericardial effusion had evidence of cardiac tamponade on echocardiogram and so pericardiocentesis was done under echocardiographic guidance. Analysis of the pericardial fluid showed it to be a lymphocytic exudative effusion which points to a tuberculous etiology. The patient's CD4 count was 186cells/mm^3 and was started on ATT and Efavirenz, Zidovudine and Lamivudine. Another patient with large pericardial effusion presented with TB meningitis. His CD4 count was 171 cells/mm^3. Studies by Steigman, Anderson, Macher et al [39] and Karve, Murali, Shah et al [38] reported that tamponade is usually associated with pericardial Kaposi's sarcoma and tuberculous pericarditis. Anderson and Virmani et al [53] reported that tamponade and constrictive pericarditis accounted for 9.5% of the cardiac deaths.

Studies done by Rerkpattanapipat, Wongpraparut, Jacobs et al [6] showed that small asymptomatic effusions do not require diagnostic evaluation and spontaneously resolve in up to 42% of patients. Pericardiocentesis is currently recommended for patients with large or poorly tolerated effusions or cardiac tamponade. Rerkpattanapipat P et al [6] and Heideneich et al[27] showed that pericardial disease in HIV

infection is often associated with shortened survival, independent of CD4 count. Jose Silva-Cardoso et al [34] reported severe pericardial effusions in 17% of patients with AIDS.

Electrocardiographic changes in the form of low voltage complexes were observed in the three patients with large pericardial effusion and their chest X-ray showed cardiomegaly.

Jose Silva-Cardoso et al [34] reported echogenic mass adherent to the visceral pericardium in 3% of the patients. All these patients had active infection in the form of infective endocarditis, pulmonary tuberculosis and meningitis. In this study, none of the patients had either pericardial masses or pericarditis on echocardiogram.

Myocardial Disease

In this study, five patients(11%) had involvement of the myocardium, of which two patients had dilated cardiomyopathy and two patients had mild left ventricular dysfunction . Rerkpattanapipat et al [6] showed that HIV is the underlying cause in 4% of the patients with dilated cardiomyopathy; Milei J et al [7] reported that dilated cardiomyopathy affects 10-20% of those with HIV infection and accounts for approximately a third of HIV related deaths. Herskowitz et al [22] in another study showed that global left ventricular dysfunction was detected by echocardiography in 15% randomly selected HIV patients.

Myocardial biopsy in patients with echocardiographic evidence of dilated cardiomyopathy showed that myocarditis was present in 83% of patients with dilated cardiomyopathy and co-infection with coxsackie virus, cytomegalovirus and Epstein-Barr virus was also noted in many cases as shown by Barbaro G et al .[37]

In this study, two patients had global hypokinesia of all the four chambers and dilated cardiomyopathy with ejection fraction of 32-36% which accounted for 4% of the patients. They had symptoms of congestive cardiac failure and opportunistic infections in the form of oropharyngeal candidiasis. One of these patients had HIV associated encephalopathy.[17] Their chest x-ray showed cardiomegaly and ECG showed sinus tachycardia and low voltage complex in one of patients with cardiomyopathy.

The CD4 counts of patients with dilated cardiomyopathy were between 100-150 cells/mm^3. These patients with dilated cardiomyopathy were started on HAART, ACE inhibitors and diuretics. There was no improvement in ejection fraction after two months of treatment. Chariot P.et al [35] showed higher frequency of dilated cardiomyopathy in patients with CD4 counts less than 100 cells/mm^3 indicating an association between the degree of immuno-suppression and development of cardiomyopathy. Apart from immuno-suppression, selenium deficiency has been identified as a cause of HIV related heart muscle disease by Barbaro G et al [37] and Rerkpattanapipat et al.[16] Longo-Mbenza et al [19]

have recently shown, in a study on African patients, that diastolic dysfunction that usually precedes systolic dysfunction is an important feature of HIV associated heart disease. Lipschultz et al [9] showed that heart failure and left ventricular dysfunction were markers of a dismal prognosis.

Endocardial Disease

In this study, Infective endocarditis was observed in one patient and that patient had history of intravenous drug abuse. The patient's blood culture grew staphylococcus aureus and echocardiogram showed vegetations over the tricuspid valve. His echocardiogram showed sinus Tachycardia. Patient's CD4 count was 244 cells/mm^3. He was treated with antibiotics. Barbaro G, Fisher SD and Pellicelli AM et al [2] showed that bacterial endocarditis in HIV infection is infrequent and appears almost exclusively in intravenous drug users with prevalence of 6.3%-34%. The low prevalence of endocardial involvement in this study may be related to the low prevalence of intravenous drug abusers in the study group.

Pulmonary Hypertension

One patient presented with pulmonary hypertension in this study. This patient's electrocardiogram showed 'P' pulmonale, right ventricular hypertrophy with strain and right axis deviation. Echocardiogram showed severe right atrial and right ventricular dilatation and severe

pulmonary hypertension. Chest x-ray showed a prominent main pulmonary trunk. The patient's CD4 count was 241 cells/mm^3 and was given symptomatic treatment. Studies by Sitbon et al [80] showed that oral endothelin receptor antagonist bosentan improved exercise tolerance and hemodynamic measurements in HIV patients. The effects of HAART on pulmonary hypertension are unknown and further studies are needed to prove its effectiveness. Recent report from the Swiss Cohort study by Zuber et al [79] showed a decrease in the pulmonary artery pressure with HAART.

Changes in the chest x-ray suggestive of cardiac disease were observed in 7 (16%) patients. All the seven patients had echocardiographically demonstrable cardiac lesions.

Electrocardiographic Changes

Sinus Tachycardia was the most commonly reported ECG abnormality in this study, seen in 18(40%) patients. Sinus Tachycardia was not only due to cardiac disease but also associated conditions like fever, anemia, pulmonary diseases, etc. Apart from being associated with fever, anemia, overt myocardial dysfunction, isolated persistent tachycardia could be an early feature of myocarditis. Low voltage complexes were seen in 4 (9%) patients of whom three patients had pericardial effusion and one had cardiomyopathy. Diffuse ST-T changes were seen in two patients. These patients did not have any cardiac lesion by echocardiogram. P Pulmonale and right ventricular hypertrophy with right axis deviation was noted in one patient with pulmonary hypertension secondary to HIV disease.

Only male patients had cardiac manifestations in this study. This may be because of the unequal gender distribution in this study. But it has been hypothesized that HIV infected females live longer than their male counterparts. Further studies are needed to validate this hypothesis.

Among the HIV positive patients with heart disease, nine patients had the disease for more than 18 months.Hence,longer the duration of HIV illness more the chances for the heart to be involved.

Individuals in the age group 28-35 years had an increased prevalence of cardiac lesions. The reason for this could be that these individuals might have been infected in their twenties and are manifesting after an incubation period.

All of the subjects were smokers and 20% were alcoholics. These risk factors for heart disease are the same as in general HIV seronegative population. There was no significant increase in incidence of cardiac illness in HIV infected individuals with these known atherogenic risk factors.

The limitations of this study are:

- Unequal representation of males and females.
- Small sample size.
- Lack of endomyocardial biopsy studies.
- Incapability of determining the etiology of pericardial effusions.

CONCLUSIONS

The prevalence of cardiac disease in HIV positive patients was 26.6% in this study.

- All patients with symptoms suggestive of heart disease did not have cardiac lesions on echocardiogram. This may be due to the fact that symptoms of respiratory diseases and anemia in HIV disease can mimic symptoms of heart disease.

- Among the various heart diseases in HIV positive patients, pericardial disease was seen in maximum number of patients (13%).

- Small asymptomatic pericardial effusions in HIV disease tend to resolve spontaneously with time and do not require diagnostic evaluation.

- Large pericardial effusions and severe dilated cardiomyopathy in HIV disease are usually associated with opportunistic infections due to severe immunosuppression.

- The prevalence of heart disease increases with duration of the HIV illness.

- Patients with heart diseases can be asymptomatic in early stages of the disease so periodic electrocardiographic and echocardiographic

evaluation should be done at regular intervals from the time of diagnosis of HIV disease.

- All HIV positive patients who had heart disease echocardiographically had CD4 counts of less that 250 cells/mm^3.
- Early diagnosis and treatment of cardiac lesions could improve the quality of life and longevity of HIV infected individual.
- Smoking does not have any increased risk for cardiac disease in HIV infected individuals when compared to non HIV general population.

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PROFORMA

HEART DISEASE IN HIV POSITIVE PATIENTS.

Sl. No. I.P. No.

Name : Age: Sex:

Occupation : Date of Admission:

Address : Date of Discharge:

DIAGNOSED HIV POSITIVE IN :

IS THE PATIENT ON HAART :

HISTORY:

01. Breathlessness
02. Chest Pain
03. Palpitations
04. Swelling of Lower Limbs
05. Abdominal distention
06. Urine Output
07. Fever
08. Cough with expectoration
09. Other symptoms

PAST HISTORY:

- H/o Diabetes, Hypertension, Tuberculosis, Bronchial Asthma
- H/o Congenital, Rheumatic, Ischemic Heart Disease

PERSONAL HISTORY:

- H/o Smoking, Alcohol Consumption
- H/o Sexual Exposure, Blood Transfusions
- Marital Status

CLINICAL EXAMINATION:

- Patient's General Condition
- Pulse: BP: Respiration: Temp:
- J.V.P.
- Pallor
- Cyanosis
- Clubbing
- Icterus
- Lymphadenopathy
- Pedal edema

CARDIAC EXMAINATION:

- Inspection
- Palpation
- Auscultation
- Other Systems
  - Respiratory
  - Abdomen
  - Central Nervous System

INVESTIGATIONS:

- Hemogram
  - Hb / PCV
  - TC
  - DC
  - ESR
  - Platelet Count
- Blood Sugar
- Urea
- Creatinine
- Sodium
- Potassium
- Urine routine examination
- Fasting Lipid Profile
- CD4 Cell Count
- Chest x-ray
- ECG
- Echo Cardiogram
- Ultra Sound Abdomen
- Other Investigations

TREATMENT GIVEN:

MASTER CHART

S. No.	NAME	Age (years) Sex	Duration Since diagnosis of HIV (in months)	Cardiac Symptoms	General Examination	Cardiac Examination	Chest X- ray (PA view)	ECG	ECHO	CD4 count Cell /mm3
1.	MUNUSAMY	29/M	22	SOB, Chest Pain Swelling of Lower limbs	Tachypneic, Bipedal Edema, BP : 90/70	JVP↑ Tachycardia, Muffled Heart Sounds, Pericardial Rub	Cardiomegaly	Low voltage complexes.	Large pericardial effusion with Tamponade.	186
2.	GOVINDHAN	41/M	12	SOB, Pricking Chest Pain.	BP: 120/80	Tachycardia	Normal	Sinus Tachycardia	Minimal Pericardial Effusion	249
3.	KUMARESAN	26/M	12	-	-	-	Normal	Normal	Normal	392
4.	NAGARAJAN	40/M	14	Chest pain (pricking type) Fever.	Tachypneic, GL.	Tachycardia	Large Left Pleural Effusion	Normal	Normal	296
5.	SELVARAJ	31/M	19	SOB, Fever	Pallor, O.C	JVP↑ Tachycardia, S1,S2 + LV S3	Pulmonary Edema	Sinus Tachycardia	Normal	350
6.	LOGANATHAN	29/M	5	-	-	W.N.L	Normal	Normal	Normal	408

7.	VENKATESAN	34/M	10	SOB, Palpitations	Tachypneic. BP:110/70	Tachycardia S1, S2, Bibasilar Rules	Normal	Sinus Tachycardia	Mild LV Dysfunction EF-55 %	189
8.	LAXMIAMMAL	30/F	12	SOB, Fever	Tachypneic, OC	W.N.L	Left pleural Effusion	Sinus Tachycardia	Normal	244
9.	RAJU	30/M	24	Pricking Chest Pain, Palpitations	BP: 120/80	Tachycardia, Pericardial Rub.	Normal	Normal	Minimal Pericardial Effusion	242
10.	KATHIJA BEGUM	26/F	10	-	GL, OC.	W.N.L	Normal	Normal	Normal	342
11.	ADIAMMAL	25/F	18	Lower limb Swelling, Decreased urine output.	OC, GL, Tachypneic Bipedal edema.	Tachycardia	Normal	Sinus Tachycardia	Normal	279
12.	RAVI	28/M	8	SOB, chest pain, lower limb swelling	Tachypneic, Bipedal Edema. BP: 100/60	JVP ↑ Tachycardia, Muffled Heart Sounds	Cardiomegaly	Low voltage Complexes.	Large Pericardial Effusion	171
13.	KANCHANA	30/F	6	SOB, Fever,	Tachypneic, Pallor, OC.	Tachycardia	Normal	Sinus Tachycardia, Difuse ST - T Changes	Normal	268

14.	VEERPANDIAN	31/M	18	SOB, Fever, Palpitations, Lower Limb Swelling, decreased urine output	Pallor, Tachypneic, Pedal edema, GL BP: 100/70	JVP ↑ Tachycardia, S1,S2,S3 PSM in Apex	Pulmonary Edema	Sinus Tachycardia	Vegetations over Tricuspid Valve.	244
15.	KUMARAVEL	37/M	10	-	-	W.N.L	Normal	Normal	Normal	389
16.	ARPUTHARAJ	32/M	4	Fever	-	-	Normal	Normal	Normal	402
17.	PANDIAN	26/M	29	SOB, Palpitations, Lower Limb Swelling, Decreased urine Output .	Tachypneic, Bipedal Edema BP: 90/60	JVP ↑ Tachycardia, S1,S2, LVS3, Bibasilar Rules	Cardiomegaly, Pulmonary Edema.	Sinus Tachycardia Low voltage Complexes	Dilated Cardiomyopathy, Global Hypokinesia, EF-32% Sever LV dys function	119
18.	ARUL	36/M	11	Fever, SOB	GL,OC.	W.N.L	B/L Infiltrations	Sinus Tachycardia	Normal	298
19.	JOHN WILLIAMS	29/M	26	SOB, palpitation	Tachypneic BP: 100/80	Tachycardia	Normal	Sinus Tachycardia	Mild L.V Dysfunction EF – 55%	151
20	MANICKAM	33/M	12	-	OC, GL	W.N.L.	Normal	Normal	Normal	428
21.	KARUPURAJ	31/M	28	SOB, Pricking	Tachypneic ,	JVP ↑	Cardiomegaly	Sinus	Large	182

				Chest Pain	OC, BP: 110/80	Tachycardia, Muffled Heart Sounds, Pericardial Rub		Tachycardia, Low voltage Complexes	Pericardial Effusion, no Tamponade.	
22.	KOKILA	25/F	2	SOB, Fever	OC,GL	W.N.L	Non homogenous Opacity right Lower zone	Sinus Tachycardia, Diffuse ST - T Changes	Normal	298
23.	VAJRAM	27/M	9	-	GL,Pallor	W.N.L	Normal	Normal	Normal	276
24.	NAZAR MOHAMMED	40/M	12	-	-	W.N.L	Normal	Normal	Normal	368
25.	SANKAR	35/M	15	-	-	W.N.L	Normal	Normal	Normal	274
26.	FATHIMA	28/F	9	-	-	W.N.L	Normal	Normal	Normal	336
27.	ANTONY	36/M	19	S.O.B., Chest pain	-	Tachycardia	Normal	Sinus Tachycardia	Minimal pericardial effusion	245
28.	RAMACHANDRAN	32/M	21	SOB, Swelling of Lower Limbs, Decreased urine output	OC, Bipedal Edema	JVP,Tachycardia	Normal	Sinus Tachycardia	Normal	406
29.	AYYANAR	27/M	27	-	Emaciated	W.N.L	Normal	Normal	Normal	212

30.	GOVINDARAJ	30/M	13	-	Pallor,GL	W.N.L	Normal	Normal	Normal	373
31.	LEELAVATHI	24/F	11	-	Pallor, Emaciated	W.N.L	Normal	Normal	Normal	291
32.	JANAKIRAM	34/M	24	-	OC	W.N.L	Normal	Normal	Normal	308
33.	BHAKIYAVATHI	28/F	14	Fever, Decreased Urine output	Pedal Edema	W.N.L	Normal	Sinus Tachycardia	Normal	252
34.	PRAKASH	41/M	11	-	-	W.N.L	Normal	Normal	Normal	388
35.	SELVAM	25/M	8	-	OC	W.N.L	Normal	Normal	Normal	352
36.	JAYAKUMAR	29/M	17	Pricking Chest Pain, Fever	G.L., Tachypneic	Tachycardia	Right Pleural effusion	Sinus Tachycardia	Normal	275
37.	JOHN PETER	25/M	14	-	OC, Emaciated	W.N.L	Normal	Normal	Normal	358
38.	ABDUL SALAM	32/M	26	SOB, Palpitations, Lower Limb Swelling, Decreased Urine output	Tachypneic Bipedal Edema BP:110/70	JVP ↑ Tachycardia, Loud P2 PSM in Apex	Cardiomegaly, Prominent Main Pulmonary Trunk, pruning of peripheral Vessels.	Sinus Tachycardia Right axis, P Pulmonale, Right Ventricular Hypertrophy .	Right atrial and right ventricular dilatation, severe Pulmonary Hypertension Tricuspid Regurgitation.	249
39.	KUPPUSAMY	29/M	14	-	-	W.N.L	Normal	Normal	Normal	414

40.	ANANDRAJ	32/M	18	-	OC,GL	W.N.L	Normal	Normal	Normal	398
41.	THIRUVENGADAM	29/M	21	-	OC	W.N.L	Normal	Normal	Normal	422
42.	VANDEVAN	36/M	13	-	-	W.N.L	Normal	Normal	Normal	378
43.	MUNIAPPAN	35/M	36	SOB, Palpitations, Lower limb swelling	Tachypneic Pedal edema, BP: 100/70	JVP ↑ Tachycardia, S1,S2, PSM in apex Bibasilar rales.	Cardiomegaly, Pulmonary Edema.	Sinus Tachycardia	Dilated cardio myopathy, Global Hypokinesia, Severe LV Dysfunction EF –36% Trivial Mitral Regurgitation	108
44.	SATHIYARAJ	31/M	9	-	-	W.N.L	Normal	Normal	Normal	458
45.	FRANCIS	33/M	14	-	-	W.N.L	Normal	Normal	Normal	302

ABBREVIATIONS

M-MALE

F- FEMALE

WNL – WITHIN NORMAL LIMITS

OC – ORAL CANDIDIASIS

GL- GENERALISED LYMPHADENOPATHY

JVP – JUGULAR VENOUS PULSE

BP- BLOOD PRESSURE

LV- LEFT VENTRICLE.

PSM- PAN SYSTOLIC MURMUR

EF – EJECTION FRACTION